

AMENDMENTS TO THE CLAIMS:

1. (Currently amended) A method for treating a connective tissue disorder ~~[which comprises:]~~ in a mammalian host, the method comprising transducing a population of target cells with a recombinant vector encoding a therapeutic protein, or a biologically active derivative or fragment thereof, and

(a) ~~generating a recombinant vector that comprises one or more DNA sequences encoding one or more genes of interest;~~

b) ~~infecting a population of *in vitro* cultured target cells with said recombinant vector, resulting in a population of transduced target tissue cells; and,~~

c) (e) ~~transplanting said transduced [target] cells [to] into the mammalian host, such that subsequent expression of [said gene or genes] the therapeutic protein, or a biologically active derivative or fragment thereof within the host reduces at least one deleterious joint pathology or indicia of inflammation normally associated with a connective tissue disorder[; wherein said gene of interest encodes one or more therapeutic genes selected from the group consisting of: interleukin 1 receptor antagonist protein; a Lac Z marker gene; soluble IL-1 receptor; soluble TNF  $\alpha$  receptor, a proteinase inhibitor; a cytokine; CTL A<sub>4</sub> FasL; and biologically active derivatives or fragments of these genes].~~

2. (Currently amended) The method of Claim 1, wherein said target cells ~~[is selected from the group consisting of]~~ are connective tissue cells ~~[ and non-connective tissue cells].~~

3. (Currently amended) The method of Claim 2, wherein said connective tissue cells are ~~[selected]~~ synovial cells ~~[from the group consisting of synovium, cartilage, tendon, ligament, skin, bone, meniscus, and intervertebral disc cells and said non-connective~~

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~~tissue cells are selected from the group consisting of hematopoietic progenitor cells, stromal cells, bone marrow cells, myoblasts, leukocytes, lymphoid cells and myeloid cells].~~

4. (Currently amended) The method of Claim 3, wherein said transduced [target] cells are transplanted at ~~[one or more locations selected from the group consisting of]~~ a joint space~~[-bone marrow or blood stream]~~ of said host.

C1  
60-5  
5. (Currently amended) The method of Claim 2, wherein said therapeutic protein is a cytokine ~~[is one or more members selected from the group consisting of IL-4, IL-10, IL-13, growth factor, and BMP]~~.

6. (Currently amended) The method of Claim 5, wherein said cytokine is BMP<sub>1</sub> ~~[is]~~ selected from the group consisting of BMP-1, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8 and BMP-9.

7. (Original) The method of Claim 6, wherein said BMP is selected from the group consisting of BMP-2 and BMP-7.

8. (Currently amended) The method of Claim [2] 5, wherein said cytokine is vIL-10.

C2  
9. (Currently amended) The method of Claim [2] 5, wherein said cytokine is growth hormone.

10. (Currently amended) The method of Claim 5, wherein said cytokine is ~~[growth factor is selected from the group consisting of]~~IGF~~[-FGF and TGF]~~.

11. (Currently amended) The method of Claim 10, wherein said ~~[growth factor]~~ IGF is selected from the group consisting of IGF-1 and IGF-2.

12. (Currently amended) The method of Claim 2, wherein said therapeutic protein is a soluble IL-1 receptor [is] selected from the group consisting of soluble IL-1 receptor Type 1 and soluble IL-1 receptor Type II.

C2  
cont  
13. (Currently amended) The method of Claim 2, wherein said therapeutic protein is a soluble TNF- $\alpha$  receptor [is] selected from the group consisting of soluble TNF- $\alpha$  receptor Type I and soluble TNF- $\alpha$  receptor Type II.

14. (Currently amended) The method of Claim 2, wherein said therapeutic protein is a proteinase inhibitor [is] selected from the group consisting of TIMP-1, TIMP-2, TIMP-3, TIMP-4[~~PAIs and serpins~~]

15. (Original) The method of Claim 2, wherein said recombinant vector is selected from the group consisting of a viral vector and a non-viral vector.

16. (Withdrawn) [~~The method of Claim 3, wherein said connective tissue cells are synovial cells.~~]

C3  
17. (Currently amended) The method of Claim 15, wherein said recombinant vector is [~~a viral vector selected from the group consisting of~~]an adenovirus [~~an adeno-associated virus, a herpes virus and a retrovirus~~].

18. (Withdrawn) [~~The method of Claim 17, wherein said retroviral vector is the group consisting of MFG and pLJ.~~]

19. (Original) The method of Claim 15, wherein said recombinant vector is a Plasmid DNA vector.

C4  
20. (Currently amended) The method of Claim 2, wherein transplantation of transduced [~~target~~] cells is by intraarticular injection.

21. (Currently amended) The method of Claim 3[16], wherein said synovial cells are autologous synovial cells.

CY  
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22. (Currently amended) The method of Claim [18] 15, wherein the [retro]viral vector is an MFG vector and the therapeutic protein, or a biologically active derivative or fragment thereof is~~[gene is selected from the group consisting of ]~~ sIL-1R [Type I, ~~and sIL-1R Type II, sTNF- $\alpha$ R Type I, sTNF- $\alpha$ R Type II, CTLA4, FasL, BMP 2, BMP 7, IGF 1, IGF 2, vIL 10, TIMP 1, TIMP 2, TIMP 3, TIMP 4, PAIs, serpins, IL 4, IL 10 and IL 13~~].

23. (Currently amended) The method of Claim 22, wherein the therapeutic protein, or a biologically active derivative or fragment thereof ~~[gene]~~ is selected from the group consisting of sIL-1R Type I, and sIL-1R Type II~~[-sTNF- $\alpha$ R Type I and sTNF- $\alpha$ R Type II]~~.

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24. (Withdrawn) ~~[The method of Claim 22, wherein the genes used are both sIL-1R and sIL-1R].~~

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25. (Currently amended) The method of Claim 22, further including the step of storing said population of transduced ~~[target]~~ cells prior to transplantation.

CS  
26. (Currently amended) The method of Claim 25, wherein said population of ~~[transfected]~~ transduced connective cells are stored in 10% DMSO under liquid nitrogen prior to transplantation.

27. (Currently amended) A method for treating a connective tissue disorder, comprising:

introducing one or more DNA sequences encoding one or more genes of interest into at least one target cell of a host by employing non-viral means selected from the group consisting of liposome, calcium phosphate, electroporation, DEAE-dextran and injection of naked DNA such that subsequent expression of said gene or genes within said host reduces at

least one deleterious joint pathology or indicia of inflammation normally associated with a connective tissue disorder[;

CS  
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wherein said gene of interest is one or more therapeutic genes selected from the group consisting of IRAP; a LacZ marker gene; sIL-1R; sTNF- $\alpha$ R, a proteinase inhibitor; a cytokine; CTLA4; FasL; and or a biologically active derivatives or fragments of these genes].

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28. (Original) The method of Claim 27, including employing a liposome selected from the group consisting of CD-cholesterol and SF-cholesterol.

29-44. (Withdrawn).

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45. (New) The method of Claim 1, wherein the therapeutic protein or biologically active derivative or fragment thereof is soluble IL-1 receptor.

C6  
46. (New) The method of Claim 5, wherein the cytokine is IL-10.

47. (New) The method of Claim 5, wherein the cytokine is BMP.

48. (New) The method of Claim 27, wherein the gene of interest is IRAP.

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